receptor with native VEGF. The Advisory Action states that, since Pötgens et al. discloses such competitive binding with their variants, this reference anticipated the claims.

In a discussion with Examiner Fitzgerald on January 3, 2000, Applicants suggested an amendment specifying that the biological activity inhibited was induction of a VEGF response. In a follow-up call on January 4, 2000, Examiner Fitzgerald agreed that such an amendment would overcome the prior art.

On the basis of the amendment and remarks presented herein, in combination with the amendment and the remarks presented in the response of September 29, 1999, we believe that this application is now in condition for immediate allowance and respectfully request the Examiner to make such a finding and pass this application to issue.

Respectfully submitted,

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APPENDIX

1. (Thrice Amended) A vascular endothelial cell growth factor (VEGF) antagonist molecule comprising a variant VEGF polypeptide, said variant polypeptide comprising an amino acid modification of at least one cysteine residue, wherein said amino acid modification inhibits the ability of said variant polypeptide to properly dimerize with another VEGF polypeptide monomer, wherein said antagonist molecule is capable of binding to VEGF receptors without significantly inducing a VEGF response, wherein said antagonist molecule is capable of inhibiting a biological activity of a native VEGF protein, wherein said biological activity is induction of a VEGF response.

2. The antagonist molecule according to Claim 1 wherein said amino acid modification is a substitution of said at least one cysteine residue with a different amino acid which is incapable of participating in a disulfide bond.

3. The antagonist molecule according to Claim 2 wherein said substitution is of the cysteine residue at amino acid position 51 and/or 60 of the native VEGF amino acid sequence.

4. The antagonist molecule according to Claim 3 wherein aspartic acid is substituted for cysteine.

5. The antagonist molecule according to Claim 4 comprising the substitution C51D.

6. The antagonist molecule according to Claim 4 comprising the substitution C60D.

7. The antagonist molecule according to Claim 1 wherein said amino acid modification is a chemical modification of said at least one cysteine residue which renders said cysteine residue incapable of participating in a disulfide bond.

8. The antagonist molecule according to Claim 7 wherein said chemical modification is of the cysteine residue at amino acid position 51 and/or 60 of the native VEGF amino acid sequence.

9. The antagonist molecule according to Claim 1 containing further amino acid modifications that do not otherwise affect the essential biological characteristics.

10. An isolated nucleic acid sequence comprising a sequence that encodes the VEGF antagonist molecule of Claim 1.

11. A replicable expression vector capable in a transformant host cell of expressing the nucleic acid of Claim 10.

12. Host cells transformed with the vector according to Claim 11.

13. Host cells according to Claim 12 which are Chinese hamster ovary cells.

14. A composition of matter comprising the VEGF antagonist molecule according to Claim 1 compounded with a pharmaceutically acceptable carrier.